FERGUSON, Mark W.J.
Appl. No. 10/722,573
January 11, 2007

RECEIVED
CENTRAL FAX CENTER
JAN 11 2007

REMARKS/ARGUMENTS

Reconsideration of this application and entry of the foregoing amendments are respectfully requested.

The title has been revised, as requested by the Examiner.

Claim 25 has been amended to include the limitation of now cancelled claim 28, 26 has been revised to define the invention with additional clarity and new claim 30 has been added. The new claim finds support throughout the application, including the claims as filed. That claims have been amended/cancelled should not be taken as an indication that Applicant agrees with any position taken by the Examiner. Rather, the revisions have been made merely to advance prosecution and Applicant reserves the right to pursue any deleted subject matter in a continuation application.

Claims 26-28 stand rejected under 35 USC 112, second paragraph, as allegedly being indefinite. Withdrawal of the rejection is submitted to be in order for the reasons that follow.

Claim 26 has been revised so as to refer to the chronic wound of claim 25.

As regards, claim 27, the Examiner's attention is directed to page 5 of the application, second paragraph, which makes it clear that IFN-γ itself is within the scope of the term "stimulator of IFN-γ" used in claim 25, from which claim 27 depends.

The Examiner's objection to the phrase "partially modified form of IFN-γ" is not believed to be well founded as a description of what is intended by the term is found on page 5, lines 7-14. From a reading of this description, an artisan would appreciate the metes and bounds of the phrase – that is all that is required.

In view of the above, reconsideration is requested.

Claims 25-29 stand rejected under 35 USC 112, first paragraph, as allegedly being non-

enabled. Withdrawal of the rejection is submitted to be in order in view of the above-noted claim amendments and comments that follow.

As the Examiner correctly notes, the pending claims are directed to a method for promoting the healing of a chronic wound using a stimulator of IFN-γ. However, the Examiner suggests that this is contrary to the experimental results provided in the specification. Applicant respectfully disagrees for the reasons that follow.

The Examiner appears possibly to be confused with regard to the specification's teaching relating to the different proposed uses of inhibitors of IFN-γ and stimulators of IFN-γ. Many of the passages cited by the Examiner relate to the anti-scarring effects of inhibitors of IFN-γ, as opposed to the pro-healing effects of stimulators of IFN-γ (as considered in the instant application).

Anti-IFN-γ treatment is indeed anti-scarring and improves the quality of the dermal architecture, however, this effect can be considered to result from a "dampening down" of the wound healing response, thereby reducing scarring that would normally occur. It will be appreciated that, in the case of chronic wounds, where healing is already delayed to a deleterious extent, the last thing that an artisan would wish to do is "dampen down" the healing response.

Instead, methods for promoting the healing of chronic wounds (as claimed in the instant application) should concentrate on "kick starting" the healing response. These are illustrated by the studies using IFN-γ itself (representing the broader class of IFN-γ stimulators). As the Examiner notes, treatment with IFN-γ gives rise to wounds that exhibit increased inflammation and angiogenesis in a dose-dependent manner.

Inflammation and angiogenesis are key processes in the normal wound healing response

that are largely responsible for the generation of granulation tissue – the mix of cells, blood vessels and extracellular matrix that is produced to fill the wound void. In chronic wounds, granulation tissue generation is either reduced or entirely absent, and this means that the wound void is unfilled, and the wound is unable to heal.

The increase in inflammation, and angiogenesis observed on administration of IFN-γ leads to the generation of greater quantities of granulation tissue. Although this has detrimental effects on the quality of the scar that is produced on healing of such wounds (as the specification and the Examiner point out), this is of minor clinical importance in the case of chronic wounds, since the primary clinical aim is to aid the healing of the otherwise non-healing wound.

The Examiner notes:

> "there is no working example of treating *chronic* wound with IFN-γ in the specification. Clearly, the present invention is based on extrapolation of the results from acute wounds. Such is not sufficient to enable the claimed invention because the result of treating *chronic* wound with IFN-γ is not predictable, as the art has established that the wound healing is extremely complicated."

The Examiner then proceeds to cite a number of documents as a means of illustrating the complexity of the wound healing process.

Although it would clearly have been desirable to include data from chronic wounds in the present specification, at the priority date of the invention, no universally accepted animal model of chronic wound healing existed. In the absence of such an accepted animal model of wound healing, two options were potentially available to those active in research in this area:

i) to conduct experiments in human patients suffering from chronic wounds; or

ii) to use the best and most accurately characterized model of animal wound healing available (acute wound models).

Clearly, the experimental use of biological compounds (such as IFN-γ) in human patients would not generally have been viewed as safe, or ethically acceptable, at the priority date of the application. As a result, and as illustrated in the cited passage from Schultz *et al.*, most researchers attempted to extrapolate results generated in acute wounds to the field of chronic wound healing.

The passage from Schultz *et al.* points out that "this approach is less than satisfactory" but does not suggest it is without merit, hence its widespread adoption by those of skill in the art. It is also worth noting that the cited article by Schultz *et al.* was published eight years after the priority date of the instant application, a period during which many advances in animal modeling (including the widespread availability of transgenic mouse models) had been made. Although extrapolation from acute wounds may have been viewed as "less than satisfactory" long after the priority date, the artisan would have realized it represented the best technique available at the time that Applicant was undertaking the studies on which the instant application is based.

In summary, while it is acknowledged that the specification contains no working examples utilizing chronic wounds, the artisan would recognize that the approach adopted by Applicant gave rise to the least possible uncertainty amongst those available at the time. Although experimentation on the part of an artisan wishing to practice the invention may be necessary, it would be recognized that Applicant had minimized the need for such experimentation to the extent possible, and that no undue burden of experimentation exists.

Reconsideration is requested.

Claims 25, 26 and 29 stand rejected under 35 USC 112, first paragraph, as allegedly lacking written description. Withdrawal of the rejection is in order in view of the above-noted revision of claim 25 to include the limitations of claim 28, which is not subject to this rejection.

FERGUSON, Mark W.J.
Appl. No. 10/722,573
January 11, 2007

Reconsideration is requested.

This application is submitted to be in condition for allowance and a Notice to that effect is requested.

Respectfully submitted,

NIXON & VANDERHYE P.C.

By: Mary J. Wilson
Mary J. Wilson
Reg. No. 32,955

MJW:tat
901 North Glebe Road, 11th Floor
Arlington, VA 22203-1808
Telephone: (703) 816-4000
Facsimile: (703) 816-4100